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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,656	10/14/2005	Ana Isabel Sanz Molinero	BJS-4982-13	5797
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/553,656

Applicant(s)

SANZ MOLINERO, ANA ISABEL

Examiner

Vinod Kumar

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08/27/07.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 11-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 October 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/14/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-10 in the reply filed on August 27, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 11-24 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was treated **without** traverse in the reply filed on August 27, 2007.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

2. An initialed and dated copy of Applicant's IDS form 1449 filed on 10/14/2005 is attached to the instant Office action.

The information disclosure statement filed 10/14/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all

other information or that portion which caused it to be listed. In the instant case, Applicant has not provided non-patent literature publications listed in the IDS filed on 10/14/2005. It has been placed in the application file, but the information referred to therein has not been considered.

Priority

3. Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy of Application No. EPO 03076086.2, filed on April 14, 2003 has been received.

Specification

The disclosure is objected to because of the following informalities:

4. The amino acid sequences on page 2, line 2; page 7, line 8; and page 8, line 10 must be referred to by their sequence identifiers, as required by 37 CFR 1.821.

Description of drawings do not have SEQ ID listed with the sequences. For example, the sequences in Figure 1 must be referred to by their sequence identifiers, as required by 37 CFR 1.821.

If the sequences appearing in the specification do not have sequence ID numbers assigned to them, then an amendment to the sequence listing will be required as well. There must not be any new matter submitted, therefore it is important to be careful to include only the sequences that are already disclosed in the current

specification. Failure to correct the deficiency will be held a non-responsive to this Office action.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example, page 7, lines 18-20; and page 9, line 1. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate action/corrections are required.

Drawings

The drawings are objected to because of the following informalities:

6. Drawings are objected to because they fail to comply with 37CFR 1.83.

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Figure 4 has sequences that are included in the specification and/or sequence listing. It is suggested to delete Figure 10.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for

consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Appropriate corrections are required.

Claim Objections

7. Claims 2 and 3 are objected to because of the following informalities:

In claims 2 and 3, line 3, it is suggested to change "corresponding wild type plants" to --plants of the same species lacking said genetic modification--. The recitation "corresponding wild type plants" does not read properly.

Appropriate action is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The preamble recites a method for modifying plant growth and development, whereas last recited method step recites "not increased metal accumulation or increased tolerance or resistance to abiotic stress". The claim does not recite all active method steps that are required to practice the instantly claimed method to achieve the instantly claimed phenotype in the plant. For example, which "genetic modification" Applicants are referring to. Does it mean that any "genetic modification" would result in modulated expression of "metallothionein protein"? The active method steps of such modification are not clear. It is unclear how one skilled in the art would practice the instantly claimed method.

Dependent claims 2-4, and 6-10 are also rejected because they fail to overcome the deficiencies of claim 1.

Claims 1 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in their recitations "modulated" in line 2 of claim 1, and "increased" in lines 4-5 of claim 1, and line 2 of claim 4, because the term "modulated" or "increased" are relative terms which render these claim indefinite. The term "modulated" or "increased" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the recitation "modulated" or "increased" is unclear as they not defined. These recitation lack a comparative basis with a plant not genetically modified.

Claims 2, 7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in their recitations "preferably" in line 2 of claims 2 and 7, line 3 of claim 9, "more preferably" in line 2 of claim 7, and "most preferably" in line 3 of claim 7, which is confusing since it is unclear if the recitations "preferably", "more preferably" or "most preferably" are intended to be claim limitations. It is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Appropriate action/corrections are required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing plant seed yield comprising transformation of a plant with a nucleic acid sequence encoding a metallothionein protein as defined in SEQ ID NO: 2, does not reasonably provide enablement for (a) a nucleic acid sequence encoding any metallothionein protein or encoding any type 2 metallothionein protein, (b) a nucleic acid sequence encoding an allelic variant or alternative splice variant of any metallothionein protein including SEQ ID NO: 2, (c) a nucleic acid encoding a functional portion of any metallothionein protein including SEQ ID NO: 2, (d) homologues, derivatives, and active fragments of any metallothionein protein including SEQ ID NO: 2, (e) increasing expression of a nucleic

acid encoding a metallothionein protein in a plant by a method other than transforming said plant with said nucleic acid, and (f) any modification in plant growth and development as a result of increased overexpression of SEQ ID NO: 2 in said plant.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims are broadly drawn to a method for modifying plant growth and development comprising introducing a genetic modification in said plant and selecting for modulated expression in said plant of a nucleic acid encoding a metallothionein protein, provided that said modified growth and development is not increased metal accumulation, increased tolerance or resistance to abiotic stress, or wherein said nucleic acid encodes a metallothionein protein of type 2 metallothionein, or wherein nucleic acid sequences encoding any metallothionein protein, and homologues, derivatives, active fragments, functional portion or splice of a metallothionein protein, or wherein said nucleic acid is an allelic variant or splice variant of a nucleic acid sequence encoding a metallothionein protein.

The instant specification, however, only provides guidance for how to make and use a nucleotide sequence (SEQ ID NO: 1) encoding the protein of SEQ ID NO: 2, in a method of producing transgenic plants and seeds with improved seed yield and increased number of primary panicles. See pages 30-35, Examples 1-5; Table 2; Figures 2 and 3.

The instant specification fails to provide guidance on how to make nucleic acid sequences encoding homologues, derivatives, active fragments, functional portion of a metallothionein protein (SEQ ID NO: 2) with the functional activity of modifying plant growth and development without increasing tolerance to abiotic stress or exhibiting increased metal accumulation. The instant specification also fails to provide guidance on how to make nucleic acid sequences which are alternative splice variants or allelic variants of a nucleic acid sequence encoding a functional metallothionein protein (SEQ ID NO: 2). The specification, page 7, lines 31-37; page 9, line 36 through the end of 1st paragraph of page 10 says:

Homologues or derivatives of a metallothionein protein comprise amino acid substitutions, deletions and/or insertions relative to the unmodified metallothionein protein having biological activity. Such homologues or derivatives are also produced by making conservative amino acid substitutions in the amino acid sequence of said unmodified metallothionein protein.

Likewise, the specification on page 10, lines 13-17 says:

Active or functional fragments of a metallothionein comprise 15, 20, 25 or 30 contiguous amino acid residues of a functional metallothionein protein.

Also, the specification on page 13, lines 22-34 says:

Alternative splice variants of a nucleic acid sequence encoding a metallothionein protein would comprise substitutions, deletions or additions of selected exons of a said nucleic acid sequence.

The specification does not provide guidance in the specification with respect to making amino acid changes in SEQ ID NO: 2.

Thus, from the guidance in the specification, it would appear that the vast majority of the amino acids in SEQ ID NO: 2 could be changed with any other amino acid.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO: 2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain biological activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making amino acid changes in SEQ ID NO: 2 protein is unpredictable. While it is known that many amino acid substitutions, additions or deletions are generally possible in any given protein the positions within the protein's sequence where such amino acid changes can be made with a reasonable expectation of success (without altering protein function) are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see for example, Wells, *Biochemistry* 29:8509-8517, 1990, see pages 8511-8512, tables 1-2; Ngo et al., *The Protein Folding Problem and Tertiary Structure Prediction*, K. Merz., and S. Le Grand (eds.) pp. 492-495, 1994; see page 491, 1st paragraph).

Furthermore, Keskin et al. (*Protein Science*, 13:1043-1055, 2004, see page 1043, abstract) teach that proteins with similar structure may have different functions. Furthermore, Thornton et al. (*Nature structural Biology*, structural genomics supplement, November 2000, page 992, 2nd paragraph bridging columns 1 and 2) teach

that structural data may carry information about the biochemical function of the protein. Its biological role in the cell or organism is much more complex and actual experimentation is needed to elucidate actual biological function under *in vivo* conditions. Thus, making and analyzing proteins with a large number of amino acid changes that also have the biological activity of increasing seed yield or plant growth would require undue experimentation.

The instant specification also fails to provide guidance on how to make nucleic acid sequences encoding allelic variants of SEQ ID NOs: 1 or 2.

The specification does not provide guidance in the specification with respect to making nucleic acid and amino acid changes in SEQ ID NOs: 1 and 2, respectively to obtain the allelic variants nor does it teach any such allelic variant sequences.

Thus, extensive teachings are required for making nucleic acids which are allelic variants of SEQ ID NO: 1 and 2, as encompassed by the claimed method.

Claims 1 and 5 are also directed to any metallothionein from any source. Claim 6 is directed to any type 2 metallothionein protein from any source. While the specification teaches a nucleotide sequences encoding SEQ ID NO: 2, it does not teach full scope of nucleotide sequences encoding other metallothionein protein that confer yield enhancement. Robinson et al. (Biochem. J., 295:1-10, 1993; see in particular, page 1, left column, lines 8-30; page 5, table 1; page 8, last paragraph in right column through the end of 1st paragraph of page 9) teach that precise function of metallothioneins remains to be elucidated. The reference further suggests that factors

(stress and non-stress related) responsible for the induction of metallothionein gene expression varies significantly in the cells of different organisms, including plants. This implies that members of metallothionein gene family are implicated in diverse cellular functions within the plant cell. Also see Chang et al. (Planta, 218:449-455, 2004; see in particular, abstract, page 449, right column; page 450, left column above materials and methods; page 452, figures 4-5; page 453, figures 6-7), who clearly suggest that class-2 metallothionein from sunflower might be involved in transport and availability of Cu^{2+} and Zn^{2+} to some apometal enzymes or apo-metal proteins.

Thus one of skilled in the art would not expect all metallothioneins including class-2 metallothioneins to cause yield and/or growth enhancement to plants. The specification does not teach which metallothioneins or class-2 metallothioneins would confer this trait and which would not. In the absence of guidance, undue experimentation would have been required by one skilled artisan at the time the claimed invention was made to isolate other metallothioneins or class-2 metallothioneins from other sources and use them in a method of obtaining plant with increased growth/and or yield.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding homologues, derivatives, active fragments, functional portion or splice variant of a metallothionein protein (SEQ ID NO: 4), or evaluate nucleic acid sequences which are alternative splice variants or allelic variants of a nucleic acid sequence encoding a metallothionein protein (SEQ ID NO: 2).

As the specification does not describe the transformation of any plant with a nucleic acid sequence encoding the metallothionein protein, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with increased plant growth and/or yield properties when expressed in a plant, if such plants are even obtainable. See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Claim 1 is directed to modifying (encompasses increasing and/or decreasing) plant growth by modulating (encompasses increasing /or decreasing) expression of a nucleic acid encoding a metallothionein protein.

The instant specification, however, only provides guidance on a method of producing transgenic plants with increased seed yield and increased number of primary panicles using a nucleotide sequence (SEQ ID NO: 1) encoding the protein of SEQ ID NO: 2. See pages 30-35, Examples 1-5; Table 2; Figures 2 and 3. The specification fails to provide guidance on a method of modifying plant growth and development other than increasing seed yield in plant transformed with a nucleic acid sequence encoding SEQ ID NO: 2. In the absence of any guidance, undue experimentation would have been required by a skilled artisan at the time the claimed invention was made to practice the instantly claimed method for its full scope.

Claim 1 is directed to modifying plant growth and development, comprising

introducing a genetic modification in said plant and selecting for modulated (increased/decreased) expression of a nucleic acid encoding a metallothionein protein.

The instant specification fails to provide guidance on a method of modifying plant growth and development comprising increasing expression of a nucleic acid sequence encoding metallothionein protein (SEQ ID NO: 2) in any manner other than transforming a plant with a nucleic acid sequence encoding SEQ ID NO: 2. The specification does not provide guidance on co-factors, or positive regulators of metallothionein, for example that makes the metallothionein gene to overexpress to produce a plant with said characteristics. The specification provides no guidance on up-stream regulatory factors, for example, that may be necessary in stimulating the overexpression endogenous metallothionein. In the absence guidance, undue experimentation would have been required by a skilled artisan at the time the claimed invention was made to determine how a plant with modified plant growth and development (increased seed yield) could have been produced by a method that comprises increasing the expression of a nucleic acid sequence encoding a metallothionein protein (SEQ ID NO: 2) without transforming the plant with a nucleic acid sequence encoding a metallothionein protein (SEQ ID NO: 2).

Claim 1 is directed to increasing expression of a nucleic acid sequence encoding any metallothionein protein in a plant results in modified growth in said plant without increasing metal accumulation or increased tolerance or resistance to abiotic stress in said plant. Claim 6 is directed to increasing expression of a nucleic acid sequence

encoding any type 2 metallothionein protein in a plant results in modified growth in said plant without increasing metal accumulation or increased tolerance or resistance to abiotic stress in said plant.

The specification provides guidance on increasing seed yield in a plant transformed with a nucleic acid sequence encoding instant SEQ ID NO: 2 as discussed above. However, the specification does not provide any guidance on the abiotic stress sensitivity of said transformed plants. Zhang et al. (Plant Science, 167:869-877, 2004) teach a type 2 metallothionein from *Typha latifolia* (a wetland plant) whose over-expression in a transgenic *Arabidopsis* plant resulted in increased abiotic stress tolerance. See in particular, page 869, abstract; page 982; figure 2; pages 983-986.

This implies that not all metallothioneins including type 2 metallothioneins would not result in increased metal accumulation and/or abiotic stress tolerance as instantly claimed. In the absence of guidance, one skilled in the art would not know how to practice the instantly claimed method for its full scope, particularly keeping in view negative limitations of said method. In the absence of guidance, undue experimentation would have been required by a skilled artisan to determine how to practice the instantly claimed method of increasing seed yield without increasing metal accumulation and/or abiotic stress tolerance.

Given the breadth of the claims, unpredictability of the art and lack of guidance of the specification, as discussed above, undue experimentation would be required by one

skilled in the art to make and use the claimed invention. Therefore, it is maintained that the claimed invention is not enabled as commensurate in scope with the claims.

10. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." *Id.*

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the

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scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Id.*

See also MPEP Section 2163, page 174 of Chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

The essential feature of the claim 1 is a nucleic acid sequence encoding a metallothionein protein which does not result in increased metal accumulation or increased abiotic tolerance when expressed in a plant. The essential feature of claim 6 is a nucleic acid sequence encoding a type 2 metallothionein protein which does not result in increased metal accumulation or increased abiotic tolerance when expressed in a plant.

The specification describes increased seed yield function of SEQ ID NO: 2 when expressed in a transgenic plant. See pages 30-35, Examples 1-5; Table 2; Figures 2 and 3.

The specification does not describe the structure of the full scope of metallothioneins including type 2 metallothioneins isolated from diverse sources. The

specification does not describe the function of metallothioneins including type 2 metallothionein from diverse sources.

There is no description of the structure required for the recited function, and no description of the necessary and sufficient elements of a metallothionein including type 2 metallothionein. Thus, Applicant's broadly claimed genus encompasses structures whose function is unrelated to the instantly claimed SEQ ID NO: 2. The specification fails to describe the function of increased seed yield or increased biomass without increasing metal accumulation or increased abiotic tolerance when expressed in a plant, for any metallothionein including type 2 metallothionein.

The only species described in the specification is SEQ ID NOs: 1, which encodes SEQ ID NO: 2. Nucleic acid sequences encoding metallothioneins including type 2 metallothioneins from diverse sources are not described, and thus their function is not described.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NOs: 1 and 2 are insufficient to describe the claimed genus.

The essential features of claim 8 are: (a) an alternative splice variant of a nucleic acid sequence encoding a metallothionein, (b) an allelic variant of a nucleic acid sequence encoding a metallothionein protein, (c) a nucleic acid encoding a functional

portion of a metallothionein protein, and (d) homologues, derivatives and active fragments of a metallothionein protein.

The specification describes seed yield function of SEQ ID NO: 2 when expressed in a transgenic plant. See pages 30-35, Examples 1-5; Table 2; Figures 2 and 3.

The specification does not describe structures of metallothionein proteins which increase seed yield but do not result in increased abiotic tolerance and/or increased metal accumulation.

The specification does not describe the structure of (a) an alternative splice variant of a nucleic acid sequence encoding a metallothionein, (b) an allelic variant of a nucleic acid sequence encoding a metallothionein protein, (c) a nucleic acid encoding a functional portion of a metallothionein protein, and (d) homologues, derivatives and active fragments of a metallothionein protein. The specification fails to describe the function of increased yield and/or biomass for sequences of (a) through (d).

There is no description of the structure required for the recited function, and no description of the necessary and sufficient elements of a metallothionein protein of SEQ ID NO: 2.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NOs: 1 and 2 are insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described the following: (a) nucleic acid sequences that encode metallothionein proteins from diverse sources, (b) nucleic acid sequences that encode type 2 metallothionein proteins from diverse sources, and (c) alternative splice variants of nucleic acid sequences encoding a metallothionein including SEQ ID NO: 2, allelic variant nucleic acid sequences encoding a metallothionein protein including SEQ ID NO: 2, (d) nucleic acid encoding a functional portion of a metallothionein protein including SEQ ID NO: 2, and homologues, derivatives and active fragments of a metallothionein protein including SEQ ID NO: 2 from diverse sources, (e) structures encompassed by (a) through (d) that result in modified growth and development in a plant without increasing metal accumulation and abiotic stress tolerance when expressed in said plant. The specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed compositions, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

Accordingly, there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing. See Written Description guidelines published in Federal Register/Vol.66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-5, and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Basel et al. (WIPO Publication No. WO 98/36084, Published 20 August, 1998, Applicant's IDS).

Claims are broadly drawn to a method for modifying plant growth and development comprising introducing a genetic modification in said plant and selecting for modulated expression in said plant of a nucleic acid encoding a metallothionein protein, provided that said modified growth and development is not increased metal accumulation or increased tolerance or resistance to abiotic stress, or wherein nucleic acid sequences encoding any metallothionein protein, and homologues, derivatives, active fragments, functional portion or splice of a metallothionein protein, or wherein said nucleic acid is an allelic variant or splice variant of a nucleic acid sequence encoding a metallothionein protein.

Basel et al. disclose a method of making a transgenic plant with increased growth and development comprising introducing and overexpressing a nucleic acid sequence encoding a metallothionein, and wherein the nucleic acid is expressed under a constitutive promoter. The reference does not disclose that said plants had increased

accumulation of metals or increased tolerance or resistance to abiotic stress. See in particular, pages 2, lines 11-23; page 9, lines 7-14; page 35, line 6; page 37, line 12; SEQ ID NO: 7.

The properties of increased seed yield and increased biomass would be inherent to the method of increasing growth and development disclosed in the reference which comprises overexpression of said metallothionein protein in the transgenic plant.

If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, rather than any distinct definition of any of the claimed invention's limitations, then preamble is not considered a limitation and is of no significance to claim construction. See MPEP 2111.02.

Also see *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1346-48, 64 USPQ2d 1202, 1204-05 (Fed. Cir. 2002) where a claim at issue was directed to a method of preparing a food rich in glucosinolates wherein cruciferous sprouts are harvested prior to the 2-leaf stage. The court held that the preamble phrase "rich in glucosinolates" helps define the claimed invention, as evidenced by the specification and prosecution history, and thus is a limitation of the claim (although the claim was anticipated by prior art that produced sprouts inherently "rich in glucosinolates").

Also see *Integra LifeSciences I Ltd. V. Merck KGaA* 50 USPQ2d 1846, 1850 (DC Scalif 1999), which teaches that where the prior art teaches all of the required steps to practice the claimed method and no additional manipulation is required to produce the claimed result, then prior art anticipates the claimed invention.

Accordingly, Basel et al. anticipated the claimed invention.

Applicant must note that homologues, derivatives or active fragments of claim 8 read on metallothionein disclosed in the reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Basel et al. (WIPO Publication No. WO 98/36084, Published 20 August, 1998, Applicant's IDS) in view of Zhou et al. (Mol. Gen. Genet. 248:318-328, 1995).

Claims are broadly drawn to a method for modifying plant growth and development comprising introducing a genetic modification in said plant and selecting for modulated expression in said plant of a nucleic acid encoding a metallothionein protein, provided that said modified growth and development is not increased metal accumulation or increased tolerance or resistance to abiotic stress, or wherein said nucleic acid encodes a metallothionein protein of type 2 metallothionein, or wherein nucleic acid sequences encoding any metallothionein protein, and homologues, derivatives, active fragments, functional portion or splice of a metallothionein protein, or wherein said nucleic acid is an allelic variant or splice variant of a nucleic acid sequence encoding a metallothionein protein, or wherein said type 2 metallothionein is from a

dicot plant species, or wherein expression of said nucleic acid encoding said metallothionein protein is driven by a constitutive promoter.

Basel et al. teach a method of making a transgenic plant with increased growth and development comprising introducing and overexpressing a nucleic acid sequence encoding a metallothionein, and wherein the nucleic acid is expressed under a constitutive promoter. The reference does not disclose that said plants had increased metal accumulation or increased tolerance or resistance to abiotic stress. See in particular, pages 2, lines 11-23; page 9, lines 7-14; page 35, line 6; page 37, line 12; SEQ ID NO: 7.

Basel et al. do not teach a nucleic acid sequence encoding an *Arabidopsis* type 2 metallothionein protein as defined in instant SEQ ID NO: 2.

Zhou et al. teach a nucleic acid sequence encoding *Arabidopsis* type 2 metallothionein protein (MT2a) which has 100% sequence identity to instant SEQ ID NO: 2. The reference further teaches that nucleic acid sequences encoding members of metallothionein proteins are differentially regulated. In particular, MT2a is overexpressed in the mature leaves and inflorescence, compared to other members of the gene family. See in particular, page 318, abstract; page 322, figure 3; page 324, figures 6 and 7; page 326, 2nd column through the end of 1st column of page 327.

At the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to modify the method of making a transgenic plant with increased growth and development as taught by Basel et al., to substitute the coding sequence encoding Basel et al. metallothionein protein with a nucleotide sequence

encoding Zhou et al. type 2 metallothionein protein to obtain a transgenic plant and transgenic seed expressing Zhou et al. metallothionein protein.

Given that Basel et al. teach that overexpressing a metallothionein protein in a plant improves growth and development and Zhou et al. teach that type 2 metallothionein proteins (MT2a, in particular, emphasis added) are highly expressed in tissues like leaf and inflorescence and, one of ordinary skill in the art would have been motivated to express Zhou et al. sequence in a plant to obtain transgenic plants having improved growth and development with reasonable expectation of success. It would have been obvious that increased growth and development would have improved yield, such as seed yield with reasonable expectation of success.

Thus, the claimed invention as a whole is prima facie obvious over the combined teachings of the prior art.

Conclusions

13. Claims 1-10 are rejected.

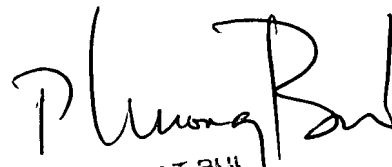
Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1638

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


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